

Epidemiologic Basis for the Asbestos Standard

by Philip E. Enterline*

The current standard for occupational exposure to asbestos is 2 fibers/cm³ averaged over an 8-hr day. A NIOSH/OSHA committee has recently concluded that the 2 fiber/cm³ standard is grossly inadequate to protect workers from asbestos-related disease, and that all levels of asbestos exposure studied thus far have demonstrated asbestos-related disease. The committee recommends that a 0.1 fiber/cm³ limit replace the current 2 fiber/cm³ standard on the grounds that this is the lowest level detectable with currently available analytical techniques. Thus a 0.1 fiber/cm³ limit is not based on epidemiological data but on the presumption that any level of exposure is disease producing.

This paper addresses the question of whether it would be possible to detect health effects of exposure below the current 2 fiber/cm³ standard. Five studies are reviewed which provide evidence on the strength of the relationship between asbestos fiber exposure and lung cancer. Calculation of sample sizes needed to be 95% certain of detecting the kind of excess probably associated with exposure to 2 fibers/cm³ suggests that epidemiology is not likely to be useful in detecting lung cancer below the current standard. Some outcome measures other than lung cancer or clinical asbestosis will be needed if observations on humans are to be used as evidence for a lowering of the present standard.

In 1938 the Public Health Service reported on chest X-rays of 541 employees in four asbestos textile plants (1). They found many cases of asbestosis where dust exposure had exceeded 5 million particles per cubic foot (mppcf), but only three doubtful cases for workers exposed at less than 5 mppcf. In their report they stated: "It would seem that if dust concentrations in asbestos factories could be kept below 5 million particles, new cases of asbestosis probably would not occur."

This recommendation was adopted by most states, The American Conference of Governmental Industrial Hygienists and eventually by many countries throughout the world. In fact, when I first became interested in asbestos during the early 1960s and visited a number of countries I was assured that they all abided by the "American Standard." That is, they all used 5 mppcf as their threshold limit value (TLV).

In 1968 the American Conference of Governmental Industrial Hygienists (ACGIH) proposed a new standard—2 mppcf or 12 fibers/cm³. In 1971 this 12-fiber standard was adopted by the Occupa-

tional Safety and Health Administration (OSHA) along with many other ACGIH standards (36 FR 10466). However, a study of two asbestos textile plants in Pennsylvania, where exposures were mainly below 5 mppcf and in many cases below 2 mppcf, revealed 14 cases of asbestosis. Partly as a result of this in December 1971 OSHA issued an emergency standard of 5 fibers/cm³ (36 FR 23207). This was made a permanent standard in 1972 (37 FR 466).

During this same period there was considerable interest in setting a dust standard for asbestos in Great Britain. In 1968 the Committee on Hygiene Standards of the British Occupational Hygiene Society (BOHS) 1968 issued a recommendation that asbestos fibers in the environment be reduced to the point where the risk of contracting asbestosis would be only 1% after a lifetime of exposure (2). Based on a review of the available evidence, and in particular a study of 290 men employed 10 years or more between 1933 and 1966 in a British asbestos textile mill where fiber exposures could be estimated, it was recommended that lifetime exposures be limited to 100 fibers/cm³-yr. Thus, for a working lifetime of 50 years this limited exposure to 2 fibers/cm³. The

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risk-exposure relationship used in the British recommendation was based on basal rales and X-ray changes, with basal rales the key symptom.

The National Institute of Occupational Safety and Health (NIOSH) took note of the British recommendation and in 1972 concurred that exposure should be reduced from 5 to 2 fibers/cm³. Before this could be acted upon by OSHA, new evidence from the same British factory used in the recommendation of the 2 fiber/cm³ standard became available which showed abnormal X-ray findings related to the lung and pleura among workers exposed at levels below 2 fibers/cm³ and in October 1975 OSHA proposed a 0.5 fiber/cm³ standard (40 FR 197). In addition to the new British data, OSHA cited another study in which 38% of 210 family contacts of former asbestos workers at Patterson, New Jersey, were reported to show X-ray changes characteristic of asbestos exposure. The actual exposure for these persons was believed to have been much lower than that in occupational circumstances. In recommending this 0.5 fiber/cm³ standard, evidence of the carcinogenic properties of asbestos was cited. Of particular importance was evidence that malignant mesotheliomas were occurring in populations where exposure was "much less than 100 fiber years," the level suggested in 1972 by the NIOSH 2 fiber/cm³ recommendation with 50 years lifetime exposure. Evidence was also beginning to accumulate which showed that lung cancer might be occurring below the exposure levels where asbestosis could be detected. A major consideration in setting the 0.5 fiber/cm³ standard appears to have been the mounting evidence that asbestos was a human carcinogen. A memorandum dated September 1975 to the Deputy Assistant Secretary of Labor for OSHA from the Director of NIOSH was cited: "multiple and consistent epidemiologic studies leave virtually no doubt that asbestos is carcinogenic in man."

In early 1976 OSHA adopted as a permanent standard the 2 fiber/cm³ standard recommended by NIOSH in 1972. This remains in effect to this day. No action has been taken by OSHA on its 1975 proposal that the permissible exposure level be dropped to 0.5 fiber/cm³. Nor has any action been taken on a 1976 NIOSH proposal that the exposure limit be dropped to 0.1 fiber/cm³.

In the fall of 1979 a NIOSH/OSHA committee was formed under the direction of the then Assistant Secretary of Labor, Eula Bingham, to review the scientific information concerning asbestos-related disease and assess the adequacy of the 2 fiber/cm³ standard. In their April 1980 report they concluded that the 2 fiber/cm³ standard is

grossly inadequate to protect workers from asbestos-related disease, pointing out that the 1968 BOHS standard upon which it was based was limited to the purpose of minimizing asbestosis and that it subsequently was shown to be inadequate for this. Second, they noted that all levels of asbestos exposure have demonstrated asbestos-related disease, and that a linear dose-response curve appears to best describe the relationship. It was noted, however, that adequate epidemiological information was not available to show the disease experience of workers exposed at levels below 2 fibers/cm³ and that any recommendation for a standard below 2 fibers/cm³ needs to be based on the presumption that an excess exists but that workers have not been followed long enough to detect a disease excess. A 0.1 fiber/cm³ limit was recommended to replace the current 2 fiber/cm³ standard on the grounds that this is the lowest level detectable with currently available analytical techniques (4).

It is important that the NIOSH/OSHA committee's recommendation of a 0.1 fiber/cm³ limit was not based on epidemiologic data. Even at 0.1 fiber/cm³ they believed that disease might occur. This principle of setting an asbestos standard at the lowest level detectable would eventually lead to a near zero permissible level and the total banning of asbestos as analytic techniques improve. This is the principle followed by the Food and Drug Administration in setting allowable concentrations of carcinogenic substances in food. It requires no epidemiologic data, other than that which might be used to classify a substance as a carcinogen in the first place. Whether this kind of basis for rulemaking in regard to occupational exposures will be upheld in the courts is uncertain in view of a recent Supreme Court decision that held that some benefit must be demonstrated when changing a standard in this way (5).

While consideration was being given to lowering the asbestos standard in the U.S., a kind of parallel but more formalized project was being carried out in Great Britain. In 1976 an Advisory Committee on Asbestos (BACOA) was established to review the risks to health arising from exposure to asbestos and to make recommendations. A final report from this committee appeared in October 1979. This report recommends a reduction in the then 2 fiber standard in effect in Great Britain to 1 fiber for chrysotile asbestos, 0.5 fibers for amosite asbestos, and a virtual banning of crocidolite asbestos (6). The committee's report is of particular interest, since the committee itself excluded persons who had already made commitments on the asbestos question and thus provides

Table 1. Historic exposure limits for asbestos in the United States.

	Limit	Source
August 1938	5 mppcf	Dreessen-Public Health Bulletin #241
Fall 1968	2 mppcf or 12 fibers/cm ³	Proposed by American Conference of Governmental Industrial Hygienists
November 1971	12 fibers/cm ³	OSHA Mandatory Standard
December 1971	5 fibers/cm ³	OSHA Emergency Standard
January 1972	2 fibers/cm ³	NIOSH Recommended Standard
June 1972	5 fibers/cm ³	OSHA Permanent Standard
October 1975	0.5 fibers/cm ³	OSHA Proposed Standard
July 1976	2 fibers/cm ³	OSHA Permanent Standard
December 1976	0.1 fiber/cm ³	NIOSH Recommended Standard
April 1980	0.1 fiber/cm ³	NIOSH/OSHA Committee Recommendation

a kind of outside look at the problem. Adequate time was available for a very thorough review of the literature both in the U.S. and abroad, along with personal visits with many of the researchers in the field. The report noted that, in Great Britain at least, improvements in dust measuring techniques in the past decade have led to a de facto tightening of the 2 fiber/cm³ standard set in 1968 of between two- and fivefold. Thus the recommended standard of 1 fiber/cm³ for chrysotile asbestos is in fact a four- to tenfold drop from the 2 fiber/cm³ 1968 standard. Whether there have also been improvements of this magnitude in dust counting techniques in the U.S. is uncertain.

The foregoing history of exposure limits for asbestos is summarized in Table 1. Against this background it is interesting to speculate whether epidemiology can make any further contribution to the setting of an asbestos standard and whether any epidemiologic evidence of health effects below 2 fibers/cm³ can be developed. Careful consideration must be given to what kinds of health effects should be looked for. OSHA considers its mandate to "set standards which most assures that on the basis of the best available evidence that no employee will suffer material impairment of health or functional capacity from occupational exposure."

Clearly an important health effect is lung cancer. Whether this can be detected at low exposure levels depends largely on what the dose-response relationship between asbestos and lung cancer truly is. The BACOA report cited three studies which model this dose-response relationship. In two of these the relationship between asbestos exposure at several levels and respiratory cancer mortality was reported—a Canadian study of miners and millers in the Province of Quebec and an American study of retired asbestos products workers (7, 8). In both of these studies there was a strong positive linear relationship between a time-weighted measure of dose and respiratory

Table 2. Some linear models for asbestos exposure and lung cancer.

Model	Slope <i>b</i> ^a	SMR predicted at 100 fibers/cm ³ -yr
McDonald (BACOA) ^b	0.062	106.2
Peto	0.078	107.8
Enterline (BACOA) ^b	0.219	121.9
Weill ^b	0.297	129.7
Peto (BACOA)	0.500	150.0
Dement	4.000	500.0

^aSMR = 100 + 100*b*.

^bResults originally reported in mppcf but converted: 1 mppcf = 3 fibers/cm³.

cancer mortality in the range of asbestos dust exposures commonly encountered in the past by workers engaged in the mining, milling, and processing of asbestos. Extrapolation to lower levels of asbestos exposure is possible from these studies if the relationship at higher dose levels can be extended to doses near zero.

The third study cited in the BACOA report is of a textile factory in Great Britain where an estimate of fiber concentrations was available along with a relative risk for respiratory cancer (9). From this it was possible, by extrapolating to zero, to determine the slope for a linear dose-response relationship. Table 2 shows the linear regression coefficients that can be calculated from these three models. In addition two studies have been added which gives data comparable to the Canadian and American studies cited in the BACOA report (10, 11), along with an update of the study of the British asbestos textile factory (12).^{*} This update reflects the changes mentioned earlier in the method of dust counting in Great Britain and which raised estimates of historic exposures from around 12 to 30 fibers/cm³. Thus,

^{*}What has been calculated for the Peto study is exposure in fibers per cubic centimeter prior to 1951 in relation to the relative risk for lung cancer after 1951.

there are a total of six studies from which estimates can be made of the regression coefficients for levels of asbestos exposure and lung cancer. It may be significant that in only three of these were fiber counts actually given by the authors, while in the others only counts of particles were given and it was necessary to convert the reported data from millions of particles per cubic foot to fibers per cubic centimeter.

Table 2 also shows the standardized mortality ratio (SMR) for lung cancer that is predicted by each study at 100 fibers/cm³ years, assuming a linear regression equation of the form:

$$\text{SMR} = 100 + b(\text{f/cc-yr})$$

It is remarkable that the estimates shown in Table 2 differ so widely, particularly in view of the fact that the extremes are fairly well documented with extensive industrial hygiene input, and deal primarily with the same type of asbestos (chrysotile).

Each of the models shown in Table 2 can be used to estimate sample sizes needed to detect a lung cancer excess in workers exposed at the current limit of 2 fibers/cm³. Using the model from the Peto paper cited by the BACOA, for example, the model is:

$$\text{SMR} = 100 + 0.05 \text{ fibers/cm}^3\text{-yr}$$

so that at 100 fibers/cm³-yr, SMR = 150.

Suppose we would like to develop an epidemiological study that would be 95% certain to detect a difference between the lung cancer risk at the present standard of 2 fibers/cm³ and the NIOSH/OSHA proposed standard of 0.1 fibers/cm³. How large would the samples need to be to detect this kind of difference? To make the problem easier, consider 0.1 fiber/cm³ as essentially an unexposed population, so that for the Peto model the problem is to distinguish between an SMR of 150 and an SMR of 100, or more simply to detect a 50% excess in lung cancer.

An easy way to approximate sample sizes needed to detect a lung cancer excess of some

specified size is to deal with proportions of deaths due to lung cancer. Suppose lung cancer makes up 5% of all deaths without asbestos exposure and using the Peto model, for example, $(0.05)(1.50) = 0.075$ or 7.5% with asbestos exposure at 2 fibers/cm³ for 50 years. The number of deaths for all causes needed to distinguish between 5% and 7.5% where the 5% represents an expected proportion based on a very large population, is given by the formula:

$$n = \frac{[Z_\alpha \sqrt{P_0 Q_0} + Z_\beta \sqrt{P_2 Q_2}]^2}{(P_2 - P_0)^2}$$

where

$$Z_\alpha = 1.645$$

$$Z_\beta = 1.645$$

$$P_0 = 0.05$$

$$P_2 = 0.075$$

Then

$$n = \frac{[(1.645)(0.2179) + (1.645)(0.2634)]^2}{(0.075 - 0.05)^2} = 1003$$

This is the number of deaths for all causes needed to be observed in each of two groups to be 95% certain of detecting a 50% excess in lung cancer caused by asbestos at 2 fibers/cm³ for 50 years in one of the groups. Table 3 shows the estimated number of deaths for each of the models shown in Table 2 along with population sizes needed in studies where average follow-up is 25 years. Identifying very many workers with 50 years exposure at 2 fibers/cm³ would be very difficult. It might be possible, however, to identify workers with 25 years exposure at about the present 2 fibers/cm³ standard. If linear relationships held, this would result in half the excess produced by 50 years exposure. In the above example this reduces the excess $(P_2 - P_0)$ to 0.0125 and about quadruples deaths and population sizes shown in Table 3. Under these conditions it is unlikely that the required sample sizes could be obtained for any but the Dement model, and perhaps the Peto (BACOA) model. Sample sizes would be considerably reduced if some standard population were used for comparison instead of a control group; however, for the small relative risks predicted by all but the Dement model, this would be risky since confounding factors such as tobacco smoking which have a great effect on lung cancer incidence would be difficult to control in such a population.

Discussion

Epidemiology using lung cancer as an end point

Table 3. Sample sizes needed to detect effects of 2 fibers/cm³ for 50 years for various models.

Model	Number of deaths needed	Approximate population needed with average 25 yr follow-up
McDonald (BACOA)	55,055	220,000
Peto	35,035	140,000
Enterline (BACOA)	4,758	20,000
Weill	2,644	10,000
Peto (BACOA)	1,003	4,000
Dement	28	110

is not likely to be very useful in providing evidence of an effect of asbestos and lung cancer at levels below the current permissible level of 2 fibers/cm³. If some outcome other than lung cancer was used, the chance of detecting an effect would be better. Clinical asbestosis is probably not a good choice since this is as rare as lung cancer. X-ray changes have been mentioned, but these do not necessarily measure the "material impairment of health or functional capacity" which seems to form the basis for government standard setting. Lung function studies have some potential for detecting early effects of asbestos exposure, and may precede X-ray changes (13). This might prove to be a better end point measure. Malignant mesothelioma also results from asbestos exposure apparently at levels below those needed to produce lung cancer and perhaps even at levels below those which either produce X-ray changes or lung function abnormalities, so that another possibility for measuring health effects at low exposure levels might be to develop case control studies for this condition.

There is some hope that epidemiologic investigations will be useful in the future in establishing new exposure limits for asbestos. However, this will probably require the use of outcome measures other than lung cancer or clinical asbestosis.

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